

### **REMARKS**

Claims 11 and 13-15, and 17 constitute the pending claims in the present application. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Rejection based on 35 U.S.C. 112, first paragraph. Claims 1, 2, 11, 13-18, 21, 21, and 23-29 are rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for a method for reducing hearing impairment caused by the platinum-containing antineoplastic agent, cisplatin, by administration of 2-thiouracil prior to cisplatin exposure, does not reasonably provide enablement for preventing hearing impairment caused by cisplatin or preventing or reducing hearing impairment caused by other chemical agents, noise, or aging. Applicants traverse this rejection to the extent it is maintained over the claims as amended.

The Office Action states that the specification does not provide guidance or a working example for preventing or reducing hearing impairment caused by chemical agents other than cisplatin; however, the Office Action speaks only to other chemical agents such as aminoglycosides, antibiotics, ototoxic diuretics, or certain quinine-like compounds. The Office Action provides no rationale for distinguishing between reducing hearing impairment caused by cisplatin and reducing hearing impairment caused by other platinum-containing antineoplastic agents.

Applicants have amended the claims such that they now recite a method for reducing or treating hearing impairment in a subject undergoing treatment with a platinum-containing antineoplastic agent, comprising administering to the subject in need of such treatment a therapeutically effective amount of a compound represented by formula I. Applicants assert that it was well known in the art at the time of filing that platinum-based chemotherapeutic agents generally cause ototoxicity. Applicants enclose herewith Exhibit A (Muldoon, L. L. et al., Clinical Cancer Research, 6, 309-315 (2000)) which states that “[platinum-based chemotherapeutic agents, such as carboplatin and cisplatin, are effective against many human tumors, but their use may be limited by a high incidence of ototoxicity.” (Abstract)

Applicants have additionally amended the claims such that they recite a compound represented by formula I wherein R<sub>1</sub> and R<sub>2</sub> taken together form a substituted or unsubstituted heterocyclyl ring having 4 to 8 members; and R<sub>3</sub> is selected from hydrogen and alkyl. Applicants assert that the claims as amended are fully enabled and therefore respectfully request reconsideration and withdrawal of this rejection.

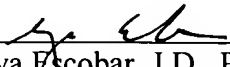
Rejection based on 35 U.S.C. 102(b). Claims 21 and 23-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Paschkis (Science, 114, 264-265). Applicants traverse this rejection to the extent it is maintained over the claims as amended.

Applicants have cancelled claims 21 and 23-28, thereby rendering this rejection moot. Applicants respectfully request reconsideration and withdrawal of this rejection.

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. Applicants believe no additional fee is due with this response, aside from the fee for the Petition for Extension of Time. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. SEPR-P01-056 from which the undersigned is authorized to draw.

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By   
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